Amendments to the Specification:

Please replace paragraph **[0090]** beginning at page 34, line 3, with the following:

--**[0090]** The core hexamer of IMSs, referred to herein as the immune modulatory sequence motif comprising a dinucleotide motif, can be flanked 5' and/or 3' by any composition or number of nucleotides or nucleosides. Preferably, immune modulatory nucleic acids comprising immune modulatory sequence motifs are oligonucleotides ranging between 6 and 100 base pairs in size, and most preferably 16-50 base pairs in size. Immune modulatory nucleic acids can also be delivered as part of larger pieces of DNA, ranging from 100 to 100,000 base pairs. IMSs can be incorporated in, or already occur in, DNA plasmids, viral vectors and genomic DNA. Immune modulatory nucleic acids can also range from 6 (no flanking sequences) to 10,000 base pairs, or larger, in size. Sequences present which flank the hexamer core can be constructed to substantially match flanking sequences present in any known immunoinhibitory sequences. For example, the IMS having the sequence ~~TGACTGTG-Purine-Pyrmidine -X-Y-Pyrimidine-Pyrimidine-AGAGATGA~~ TGACTGTG-Purine-Pyrimidine -X-Y-Pyrimidine-Pyrimidine-AGAGATGA (SEQ ID NO:298), comprises the flanking sequences TGACTGTG and AGAGATGA. Another preferred flanking sequence incorporates a series of pyrimidines (C, T, and U), either as an individual pyrimidine repeated two or more times, or a mixture of different pyrimidines two or more in length. Different flanking sequences have been used in testing inhibitory modulatory sequences. Further examples of flanking sequences for inhibitory nucleic acids are contained in the following references: U.S. Patent Nos. 6,225,292 and 6,339,068; Zeuner *et al.*, *Arthritis and Rheumatism*, 46:2219-24, 2002.--

Please replace paragraph **[0092]** beginning at page 35, line 4, with the following:

--**[0092]** A previously disclosed immune inhibitory sequence or IIS, was shown to inhibit immunostimulatory sequences (ISS) activity containing a core dinucleotide, CpG. U.S. Patent 6,225,292. This IIS, in the absence of an ISS, was shown for the first time by this invention to

prevent and treat autoimmune disease either alone or in combination with DNA polynucleotide therapy. This IIS contained the core hexamer region having the sequence AAGGTT (SEQ ID NO:28). That sequence is referred to herein as an immune modulatory sequence or IMS. Other related IISs with a similar motif included within the IMSs of this invention are:

1. 5'-purine-purine-[X]-[Y]-pyrimidine-pyrimidine-3' IMSs containing GG dinucleotide cores: GGGGTT (SEQ ID NO:25), AGGGTT (SEQ ID NO:26), GAGGTT (SEQ ID NO:27, AAGGTT (SEQ ID NO:28), GGGGCT (SEQ ID NO:29), AGGGCT (SEQ ID NO:30), GAGGCT (SEQ ID NO:31), AAGGCT (SEQ ID NO:32), GGGGTC (SEQ ID NO:33), AGGGTC (SEQ ID NO:34), GAGGTC (SEQ ID NO:35), AAGGTC (SEQ ID NO:36), and so forth;

2. 5'-purine-purine-[X]-[Y]-pyrimidine-pyrimidine-3' IMSs containing GC dinucleotide cores: GGGCTT (SEQ ID NO:37), AGGCTT (SEQ ID NO:38), GAGCTT (SEQ ID NO:39, AAGCTT (SEQ ID NO:40), GGGCCT (SEQ ID NO:41), AGGCCT (SEQ ID NO:42), GAGCCT (SEQ ID NO:43), AAGCCT (SEQ ID NO:44), GGGCTC (SEQ ID NO:45), AGGCTC (SEQ ID NO:46), GAGCTC (SEQ ID NO:47), AAGCTC (SEQ ID NO:48), and so forth;

3. Guanine and inosine substitutions for adenine and/or uridine substitutions for cytosine or thymine can be made as set forth based on the guidelines above.--

Please replace paragraph **[0144]** beginning at page 51, line 1, with the following:

--**[0144]** Based on the results with the IMS oligonucleotide demonstrating the benefit of the GpG sequences in reducing disease severity and in producing a Th2 shift in the autoreactive T cell population, we have created a modified vector incorporating GpG sequences within the vector backbone. We began with the pVAX1 vector (SEQ ID NO:297) (Invitrogen, Carlsbad, CA) which is the plasmid vector predominantly used in our EAE experiments, and which has been designed to meet all of the regulatory requirements for use in humans. We then examined the vector for CpG motifs that match the known human CpG motif consensus for immune

stimulation, that is Pu-Py-C-G-Py-Py. We determined that on one strand of pVAX1, there are 16 such CpG elements. Using site-directed mutagenesis we modified 12 of those sites as summarized on Table 1. The remaining CpG sites occurred within important control regions of the vector and, therefore, were not modified. Where possible the C in the CpG motif was changed to a G to match the sequence motif of the GpG oligo sequences used in the IMS oligonucleotide. This was done at four of the 12 modified sites. The other eight sites were modified not to a GpG but in such a way that the C within the CpG motif was changed to either an A or a T. In this way, the potentially Th1 driving immunostimulatory CpG motif was removed. The vector thus constructed has been named pBHT1.--

Please cancel the present "SEQUENCE LISTING", pages 1-60, submitted October 20, 2005, and insert therefor the accompanying paper copy of the Substitute Sequence Listing, page numbers 1 to 75, at the end of the application.